Correction dosing

- Replaces sliding scales
- Always give dose to cover food to be eaten
  - Dose dependent upon carbohydrate intake
  - Add extra Humalog units to cover additional food intake or correct for high blood sugar

Type 2 Diabetes

Type 2 Diabetes

- Obesity driven
  - Not all obese teens have diabetes
- Treatment is prevention
  - Lifestyle changes
  - Weight control and exercise
  - Appropriate for all overweight children
    - Limit TV and video time
    - Limit junk food

Incidence: Type 2 Diabetes

- Incidence is increasing
  - Incidence parallels the increasing obesity of children and teens
- Type 2 diabetes is the more common in African-American, Native American, Pacific Islander, and Hispanic children and teens
  - Genetic predisposition compounded by lifestyle
- Type 2 diabetes is caused by diet and lifestyle
  - Excess caloric intake, inadequate exercise
  - Obesity

Etiology

- Genetic factors are poorly understood in most groups
  - Probably polygenic, specific loci have been implicated in certain ethnic groups
- Environmental factors are probably similar to adults
  - Obesity and sedentary lifestyle contribute to peripheral insulin resistance, compounded by decreased insulin secretion and increased hepatic gluconeogenesis

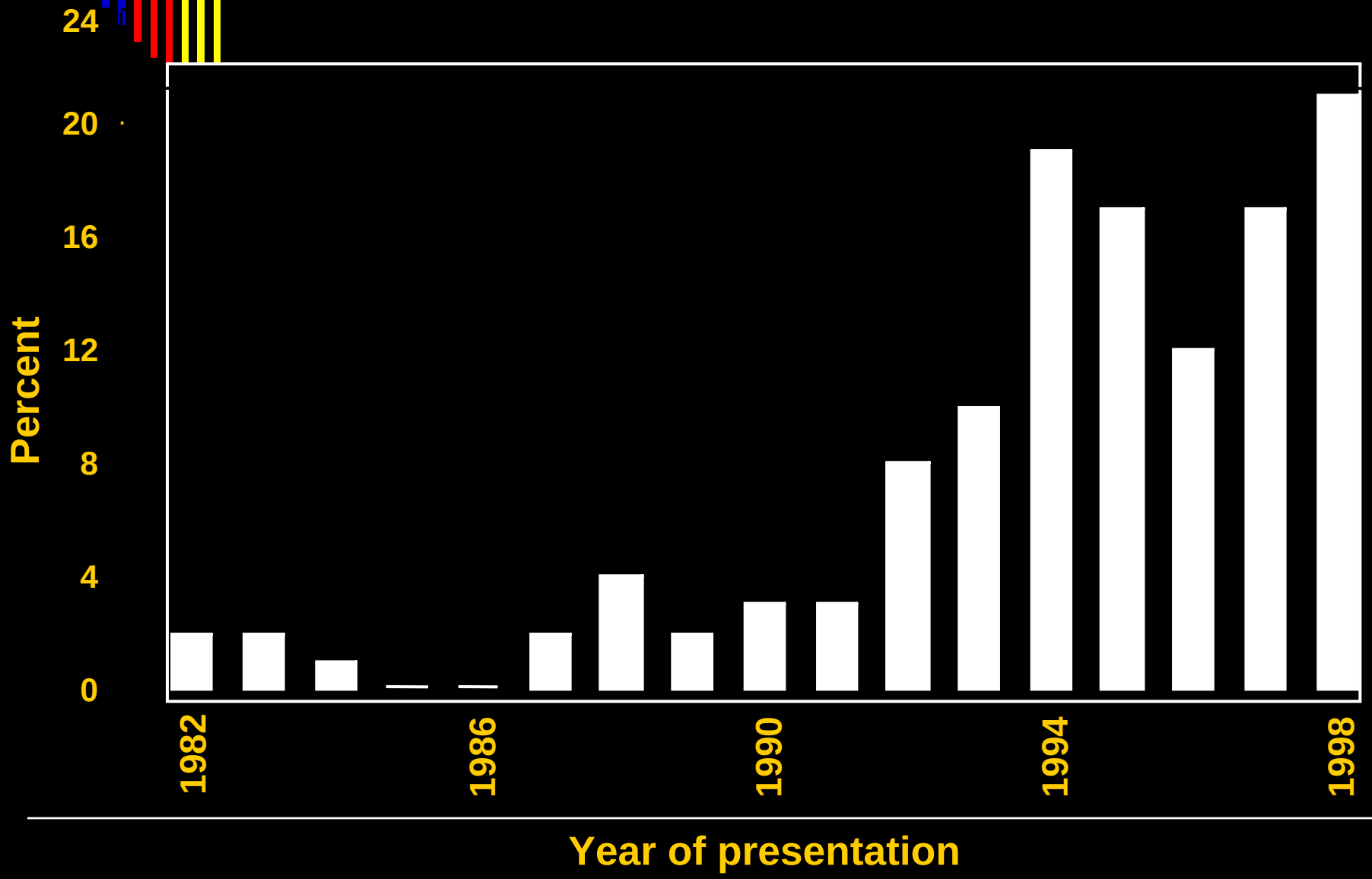
Etiology

- Puberty exacerbates incidence
  - GH is counter-regulatory hormone and increases peripheral insulin resistance
  - Insulin activity is 30% lower in Tanner 2-5 adolescents vs children and adults
- Focus on pubertal and peripubertal children (> 10 years of age)
  - Type 2 has been reported in children as young as 4 yrs

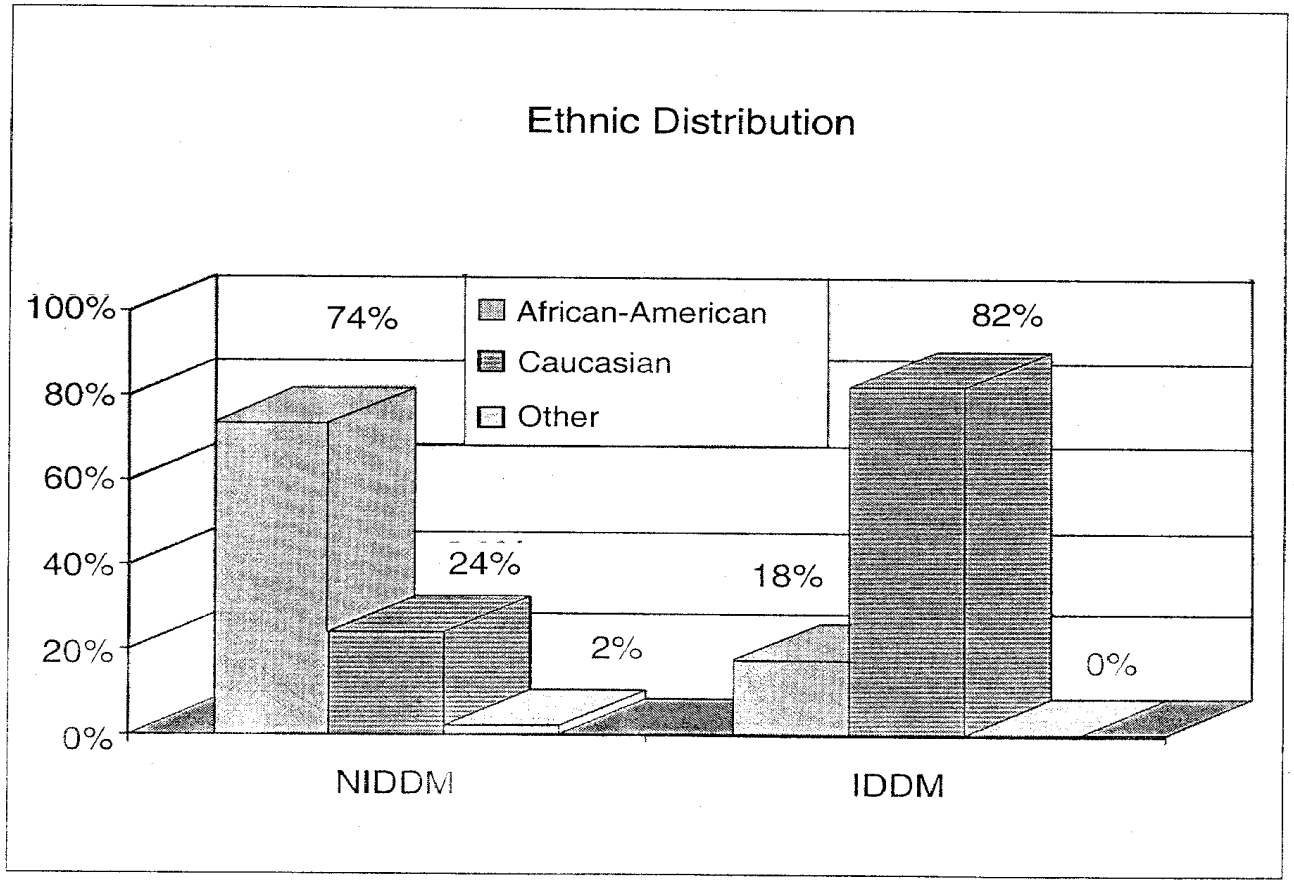
Childhood Obesity

- Prevalence of overweight children 1970-2000
  - 6-11 year olds: increased from 4% to 15%
  - 12-19 year olds: increased from 5% to 15%
- Prevalence of overweight children 1960-1980's remained constant at about
  - NHANES data, BMI>95% for age and gender

Type 2 diabetes mellitus in Cincinnati, OH



Type 2 DM and Ethnicity



Pihoker et al - 1998

Progression of Type 2 Diabetes

⇑ Insulin resistance → ⇑ hyperinsulinism

↓

↓ suppression of hepatic gluconeogenesis

↓

Fasting and post-prandial hyperglycemia

↓

Downregulation of insulin receptors &
impairment of post-receptor events

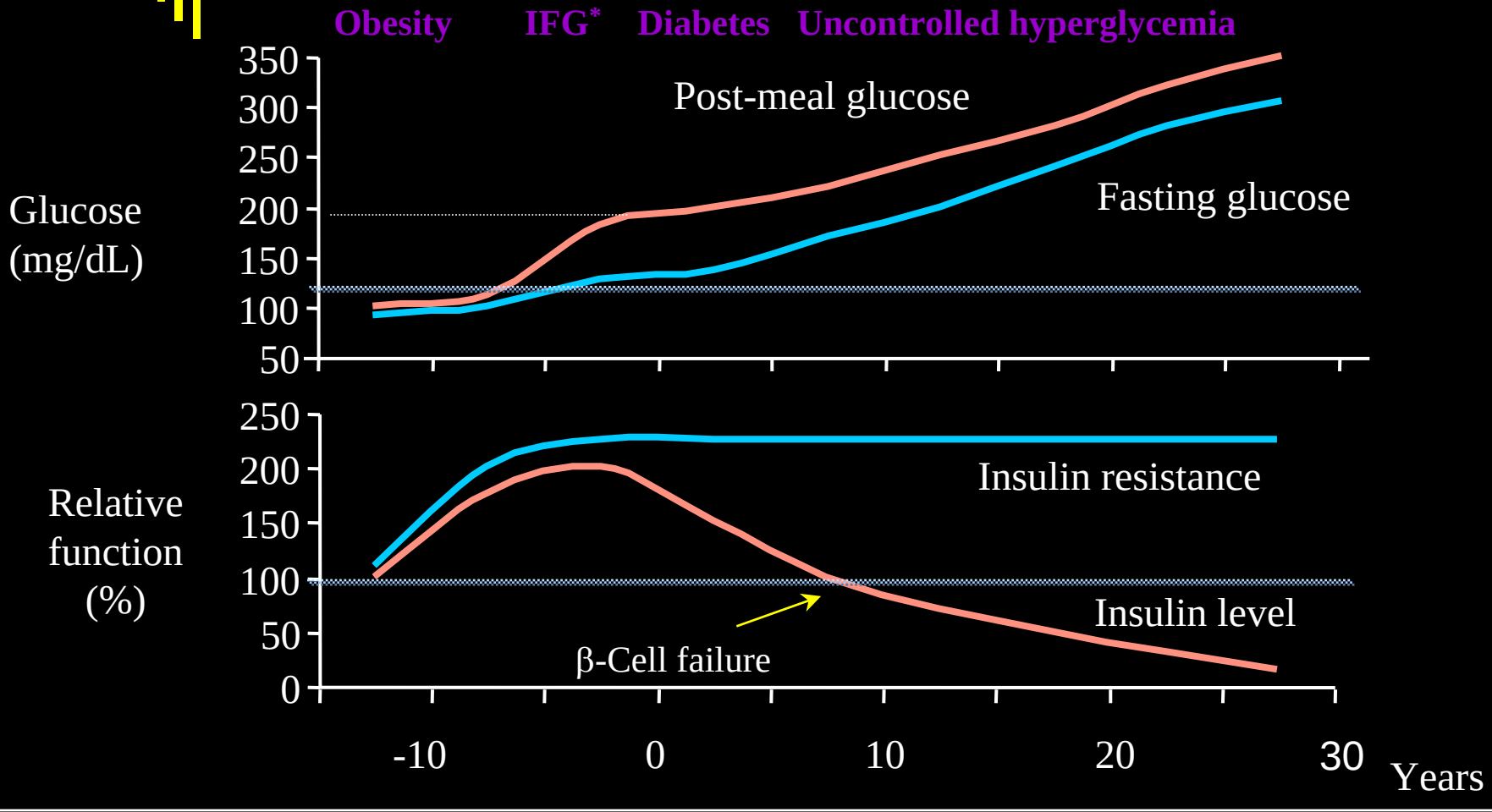
↓

⇑ Hyperglycemia → ⇓Insulin secretion

↓

Type 2 diabetes

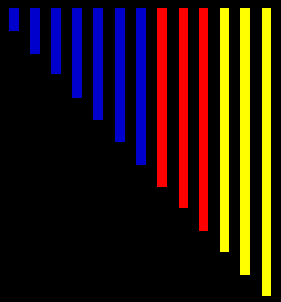
Natural History of Type 2 Diabetes



*IFG=impaired fasting glucose.

Adapted from International Diabetes Center (IDC), Minneapolis, Minnesota.

The Metabolic Syndrome of Insulin Resistance



Endothelial Dysfunction

Complex Dyslipidemia
Inc TG, sdLDL
Dec HDL

Systemic Inflammation

Insulin Resistance

Disordered Fibrinolysis

Athero-sclerosis

Hypertension

Type II Diabetes

Visceral Obesity

Adapted from the Consensus Development Conference of the American Diabetes Association. *Diabetes Care* 1998;21:310-314.
Pradhan AD et al. *JAMA* 2001;286:327-334.

Type 1 vs Type 2

- At presentation, type is not always clear
  - Type 1 accounts for 25-85% in most populations
  - Type 1 is immediately life threatening if not treated
  - Type 2 may present with ketosis (25%) and even DKA
- Laboratory testing may separate types
  - Insulin and c-peptide levels
  - autoantibodies

Diagnosis

- Little dilemma in lean or very young child
- Overweight adolescent or older school age child without DKA
  - Before administering insulin, draw C-peptide, insulin and glucose levels
  - Check antibodies
    - anti-islet cell, GAD 65, anti-insulin
    - results will take 1-2 weeks
  - Initiate therapy based upon clinical suspicion

Pharmacologic Therapy for Type 2 Diabetes

- Biguanides- (metformin)
- Insulin- (long, intermediate, short, very short, analogues, inhaled)
- Sulfonylureas- (glyburide, glipizide, glimepiride)
- Short acting Insulin Secretagogues- (repaglinide, netaglinide)
- Alpha Glucosidase Inhibitors- (acarbose, miglitol)
- Thiazoledinediones- (rosiglitazone, pioglitazone)

Oral Therapy

- Decrease glucose production
  - Biguanides: metformin
  - Thiazolidinediones: avandia, actos
- Increase insulin secretion
  - Sulfonylureas: glyburide
  - Meglitinides: prandin
- Increase peripheral glucose uptake
  - Thiazolidinediones: avandia
  - Biguanides: metformin
- Decrease intestinal glucose absorbtion
  - alpha-glucosidase inhibitors: precose

Biguanides (Metformin)

- Mechanism: decrease hepatic glucose production and improve peripheral insulin sensitivity
  - **Side effects: nausea, abdominal cramps, diarrhea**
- Contraindications: renal failure, hepatic failure, congestive heart failure, alcoholism
  - **Hold for dehydration, iodinated contrast studies**
- Advantage: little hypoglycemia, weight neutral
- Indications: Type 2 DM, PCO, Insulin resistance

Insulin Therapy in Type 2

- Initially:
  - **Severe hyperglycemia, ketonuria**
  - **Protect teen from DKA while determining the type of diabetes**
  - **When other medications contraindicated, e.g. liver disease or chemotherapy, or peri-operative**
  - **Pregnancy**
- Later
  - **When β cell function no longer adequate and oral therapy is failing**

Lifestyle Therapy

- First line of therapy
  - Potentially prevent type 2 diabetes in some teens??
- Nutrition
  - No medication will control blood glucose in the face of uncontrolled eating
  - Must have access to pediatric/adolescent nutritionists
  - Unlike current approach to type 1 diabetes, fat intake probably should be addressed initially
- Exercise
  - Increase peripheral glucose utilization by muscle, decrease body fat

Screening Children and Adolescents: Who?

- Children over 10 yrs or in puberty with the who are overweight:
  - BMI > 85% for age and sex, weight for height > 85th%, weight >120% ideal for height
- And have 2 of the following risk factors
  - Family history in first or second degree relative
  - American Indian, African-American, Hispanic, Asian/Pacific Islander
  - Signs of insulin resistance: acanthosis nigricans, PCOS, hypertension, dyslipidemia

Screening Children and Adolescents: How?

- Frequency: every 2 years
- Preferred test is the fasting plasma glucose

- Consider also:
  - 2 hour post prandial plasma glucose
    - may be abnormal before the fasting plasma glucose

Consensus statement from ADA, Pediatrics (/2000) 105: 671

“Pre-Diabetes”

- Impaired glucose tolerance
  - 2 hour PG ≥ 140 mg/dl and < 200 mg/dl
- Impaired fasting glucose
  - FPG ≥ 110 mg/dl but <126 mg/dl
  - fasting glucose is elevated but not diagnostic of diabetes

Summary

- Incidence of type 2 diabetes in the pediatric population is increasing and it will become a significant source of morbidity and financial burden on our society – worldwide
- Prevention involves changing lifestyles and environment of our children and teens
- Treatment options are the same as those available for adults but with little or no research into safety and efficacy of these drugs in pediatric population

Treatment

- Prevention
- Insulin
  - Pro
    - Protect from DKA if child has type 1 while awaiting clarification of diagnosis
    - Impact of disease upon
    - Complete education
  - Con
    - Weight gain
    - Risk of hypoglycemia
    - Complexity

Medical Therapy: Insulin

- Approved for use in children
  - lots of experience with children
- Risk of severe hypoglycemia
- Significant potential for weight gain
- Increased need for monitoring

Medical Therapy: Metformin (glucophage)

- FDA approved for use in children/teens > 12 yrs for diagnosis of type 2 diabetes
- Side effects:
  - Low risk of hypoglycemia
  - GI side effects are generally well tolerated if dose is increased gradually
  - Weight neutral; perhaps some weight loss (5kg)
- Check creatinine before starting and q year
- Hold for IV contrast or dehydration
- Consider pregnancy issues

Medical Therapy: Oral Agents

- No others approved for children
  - Sulfonylureas: most experience in adults, good safety record
- Limited experience and limited studies
  - Unknown or unanticipated side effects
  - Haptotoxicity
- Use with caution and informed consent of family until more study data is available

Prevention

- Prevention is key
  - Delay onset in many cases, possibly eliminate in some
- Weight control
  - Exercise
  - Dietary: caloric and fat intake
  - Lifestyle: -48% vs untreated control
- Medications
  - Metformin: -31% vs untreated control

Medical Treatment of Obesity

- Zenical® (orlistat)
  - Approved for use by children and teens
  - Non-systemic lipase inhibitor, inhibits absorption of fat
    - Start after patient has had some success with diet alone (2.5 kg/week times 4 weeks); discontinue if not lost 5% body weight over 12 weeks; long term therapy limited to 2 years
    - Side effect of fat soluble vitamin deficiency, flatulance, diarrhea
- Bariatric surgery
  - Lifelong change in eating habits
  - Pregnancy?

Simple Start

- Eliminate sodas and restrict juice
  - Substitute fruit and vegetables
- Smaller portions
  - Allow seconds if hungry
  - Don’t skip meals
- Limit trips to MacD’s, Burger King, etc
  - When eating there, get smaller meals

Complications

- Same complications that adults face Cardiac disease
  - Neuropathy
  - Nephropathy
- Will the complications be more severe?
  - Earlier age of onset?????
  - Predisposition to be worse????

Long Term Issues

- Aggressively maintaining control
  - Are the adult paradigms appropriate?
  - Hgb A_{1C}
  - Blood sugar testing
  - Weight control
- Management of lipid abnormalities
- Monitoring for cardiac disease at earlier ages
- Management during pregnancy

Summary

- Prevention of type 2 diabetes = Prevention of Obesity
  - Absolutely necessary for us as a society
  - Behavioral changes, start now with simple steps
  - Need studies of medications to treat obesity in children and teens
- Treatment of type 2
  - Need studies of medications
    - Teens are not just little adults
  - Entire family needs to commit to treatment
  - Mental health issues and support